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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,465	WHITSETT ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *1-38,41 and 43-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39,40 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/31/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group IV claims 39, 40, and 42 in the reply filed on 27 April 2006 is acknowledged. The traversal is on the ground(s) that the restriction requirement is improper. Applicants argue that all of the claims in Groups III-VII involve the same basic method, and that said groups are merely a Markush group based upon claim 40 which depends from claim 39, which was not listed in the restriction requirement. Applicants continue that the Examiner is required to examine all the members of a Markush group if a serious burden would not be on the examiner. Applicants continue that the art is a very well define, relatively small field and that the MPEP supports a search all of the groups if it again will not place a burden on the examiner. Applicants continue that the Examiner has indicated that either 514 or 530 classes would be needed to search for the claimed inventions of Groups III-VII. Applicants continue to argue that an enourmous cost would be burdened on the applicant which is a nonprofit Children's hospital. This is not found persuasive. To begin, the Examiner was in error in the restriction requirement, by not listing claim 39 as the linking claim for groups III-VII. As the applicant has pointed out though, claim 39 would have been the linking claim for Groups III-VII, and for the purposes of this office action, will be considered as such. Thus the elected invention will include claim 39, on top of claims 40 and 42. Further, Groups III-VII are divergent inventions that would require and undo burden on the Examiner to search each invention. Though the basic method is the same, it is the implementation of said method that requires a significant search to examine each field of technology covered in Groups III-VII. The administration of an antibody, protein, or nucleic acid via liposome, adenovirus, or retrovirus is vastly different fields of technology, and each is covered by a different art unit within the

USPTO. To argue that they are similar is not persuasive, since each field has vastly different types of technological requirements regarding administration, efficacy, enablement, and manufacture. The argument regarding the cost of prosecuting each of the restricted inventions further is not persuasive, since the MPEP states that cost is not a factor regarding the burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-38, 41, and 43-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 27 April 2006.

3. Claims 39-40 and 42 are examined in the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 39, 40 and 42 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, and 8 of U.S. Patent No. 6,838,428 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are similar to said patented claims. Said patented claims teach a method of treating a pulmonary disease comprising administereing a composition comprising mammalian surfactant protein-D protein into a human, and further comprising the administration of mammalian surfactant protein-C protein. The instant claims recited only the administration of mammalian surfactant protein-C protein. However it would have been obvious to administer mammalian surfactant protein-C protein singly since said patent discusses the benefits of administering each or both of mammalian surfactant protein-C protein or mammalian surfactant protein-D protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39, 40 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 39, 40, and 42 are drawn to a method of treating pulmonary disease in a subject comprising the administration to a subject in need of such treatment a therapeutically effective amount of a formulation comprising a SP-C therapeutic, wherein said therapeutic is a. SP-C protein.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The breadth of the claims encompasses treating any subject with any amount of an isolated SP-C protein. This embodiment reads on protein therapy.

Whereas the nature of the invention is a method of treating a patient suffering from pulmonary disease, a review of the current art teaches that the field of protein therapy is unpredictable. At the time the invention was made, successful implementation of protein therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by several reviews. Brown (2005, Expert Opinion Drug Delivery, Vol. 2(1), pgs. 29-42) discusses the many challenges that surround protein delivery and therapy. Brown teaches that proteins are commonly delivered by three routes: oral, nasal, and pulmonary (pgs. 31-33). Specifically, each has it's own challenges, with oral delivery requiring the avoidance of proteolytic enzymes and the absorbance of relatively large molecules (proteins) through a membrane that is designed to actively uptake only single amino acids, dipeptides or tripeptides (pg. 31 col. 2 parag. 2). Nasal delivery is hampered by a low bioavailatibility of the medic being delivered due to the limited area that can absorb the therapeutic. Brown teaches that low molecular weight moieties will be the most successfully for delivery via the nasal pathway, with doses from 0.2 to 400 ug (pg. 33 col. 1 parag. 3). Regarding pulmonary delivery of proteins, the main challenge is obtaining effective systemic delivery via the lungs to the alveoli or deep lung (pg. 33 col. 1 last 2 lines bridge col. 2 line 1). Brown teaches that insulin has been an exemplary protein for delivery via the pulmonary route, but that "formulating proteins such that they maintain their stability and that they are delivered within their efficacious and safe target doses remains a challenge" (pg. 39 col. 2 parag. 3).

Regarding the issue of delivery a protein to the body for treatment significant issues arise especially when the protein is produced recombinantly for treatment. The breadth of the claims encompasses the recombinant manufacture of an SP-C protein (see Spec pg. 7 parag. 21). Hayes

et al. discuss this in detail (1997, Clinical Immunology and Immunopathology, Vol. 83, pgs. 1-4). Hayes teaches specific endogenous mechanisms that exist to interfere with the delivery of proteins, mainly neutralizing antibodies (pg. 3 col. 2 parag. 6-7 bridge col. 1). Hayes continues that toxicology studies are important to determine the risk of systemic exposure to a recombinant protein, and that "artificial administration of a recombinant protein in a disease state cannot mimic the normal endogenous milieu at the site of disease or in normal tissue, where no effect is usually desired" (pg. 1 col. 2 last sentence bridge pg. 2 col. 1 lines 1-2). Hayes continues that a protein is often injected at a high dose causing exaggerated pharmacodynamic effects which can be adverse, and that many recombinant proteins are pluripotent the desired effect has limited specificity (pg. 2 col. 1 parag. 1-2).

The working examples provided by the instant specification teach the creation of SP-C -/- transgenic mice (pg. 59), analysis of lung morphology and dynamics (pgs. 64-68), and analysis of phospholipids, cytokines, and metalloprotienases (pgs. 68-69). The instant specification has gone about dissecting and examining how a deficiency of SP-C results in lung abnormalities as they relate to inflammation, pulmonary function, and resistance in the lung. However, the specification only provides the skilled artisan with the creation of said transgenic mice and detailed analysis of phenotypes that arise from a disruption in SP-C. The instant specification does not provide the skilled artisan with any guidance of treating a pulmonary disease in a subject by administering a SP-C therapeutic. While the specification has addressed the effector molecules that result in the phenotype observed in the disclosed SP-C knockout mice, the specification is silent with regard to the signal transduction mechanisms that would guide the skilled artisan to fully enable the treatment of any pulmonary disease. Further the transgenic

mice disclosed have complete ablation of SP-C, whereas a human subject for example, would conceivably still have SP-C produced and have established signal transduction pathways based upon its production. The jump from a transgenic mouse to a treatment in a human is not provided by the instant specification that would account for such a disparity.

It should be noted that U.S. Patent 6,838,428 B2 (as discussed above and below in the 102(e) rejection) teaches the administration of surfactant protein-D for the treatment of a pulmonary disorder. The specification of the '428 patent teaches how SP-D can treat a pulmonary disorder, but does not discuss how SP-C, nor any mechanism concerning SP-C would treat a pulmonary disorder. The '428 patent contemplates the dual administration of SP-D and SP-C. The instant specification does not contemplate the administration of SP-D, only SP-C for the treatment of a pulmonary disorder, and thus a complete lack of enablement is made concerning SP-C treatment. The instant specification deals mainly with characterizing the function and action of SP-C, unlike the established role of SP-D. Given that the instant specification teaches the skilled artisan only the basic role and function of SP-C in a transgenic knockout animal, and no teachings what so ever concerning in vivo treatment with SP-C, the complete lack of enablement regarding claims 39, 40 and 42 is proper.

In view of the unpredictability of the art of protein therapy, a skilled artisan would require specific guidance in the instant disclosure to make and use the full scope of the claimed embodiment. Wherein the instant specification provides specific guidelines for SP-C knockout mice, the instant specification however, has not provided any relevant teachings, guidance, or working examples that teach or otherwise correlate to a method of treating pulmonary disease in a subject comprising administering an SP-C protein therapeutic. The specification has failed to

provide any guidance or working examples that correlate administration of said protein. One of normal skill in the art would not be able to rely on the state of the art of *in vivo* protein therapy to practice the claimed method in view of the lack of disclosure regarding a method of treatment in the instant specification. Thus in view of the lack of guidance and direction provided by the specification for protein therapy in any subject, it would have required one of skill in the art undue experimentation to make and use the method as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-40, and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,838,428 B2

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 39, 40, and 42 are drawn to a method of treating pulmonary disease in a subject comprising the administration to a subject in need of such treatment a therapeutically effective amount of a formulation comprising a SP-C therapeutic, wherein said therapeutic is a. SP-C protein.

U.S. Patent 6,838,428 B2 (the '428 patent) teaches a method for the treatment of pulmonary disease comprising introducing a composition consisting essentially of mammalian surfactant protein-D (claim 1), and further comprising the administration of surfactant protein-C (claim 8). As discussed above, the '428 patent contemplates and teaches the administration of SP-C, whereas the instant specification teaches the creation of a SP-C knockout mouse, and does not contemplate the administration of SP-D. Therefore the '428 patent is applied as prior art and is anticipatory over claims 39, 40, and 42.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 1-571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David A. Montanari, Ph.D.

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER